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RESEARCH ARTICLE

EVALUATION OF THE ACUTE TOXICITY, ANTI-INFLAMMATORY AND ANALGESIC ACTIVITIES OF FOUR PLANTS USED IN THE BENINESE PHARMACOPOEIA (ANNONA SENEGALENSIS, SARCOCEPHALUS LATIFOLIUS, COMBRETUM GLUTINOSUM AND DETARIUM MICROCARPUM)

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Abstract

Inflammation and pain are a common feature of almost all non-communicable diseases. Annona senegalensis, Sarcocephaluslatifolius, Combretum glutinosum and Detariummicrocarpum have been traditionally used to treat different types of diseases. This study aimed to evaluate in-vivo anti-inflammatory and analgesic activities of these plants extracts, as well as their acute toxicity. The hydroethanolic extracts of the leaves were used for in-vivo tests on Wistar rats. The anti-inflammatory activity was evaluated by the 2% formalin-induced edema test, while the analgesic activity was evaluated by the acetic acid test. The acute toxicity of the crude hydroethanol extract was evaluated by oral administration of the extract to Wistar rats. A single dose of 2000 mg/kg body weight was administered and the effects on biochemical parameters were evaluated. The two plants tested showed a significant analgesic activity with a percentage of inhibition of cramps of 85.37 % for D. microcarpum and 87.37 % for A.senegalensis compared to aspirin which is 45.07%. The percentage of edema inhibition at 100 mg/kg reached 37.47 % for Detariummicrocarpum and 68.0 % for Annona senegalensis against 34.10 % for diclofenac. The toxicity test performed on rats by the oral route at a dose of 2000 mg/kg body weight showed no adverse effects and no deaths during the 14 days of observation.

Introduction:-

Inflammation is a complex physiological process associated with pain as a secondary process to inhibit the spread of infection. It is characterized by the formation of edema, redness and fever(Faujdaret al., 2016; Rathsmanet al., 2012). Steroidal and nonsteroidal anti-inflammatory drugs are used in the chemical therapy of inflammation-related diseases(Singh et al., 2016; Confortiet al., 2009). Nonsteroidal anti-inflammatory drugs are the first-line agents used to reduce harmful events associated with inflammation. Pain is an unpleasant and emotional experience associated with tissue damage, and it is frequently associated with inflammation(Bihaniet al., 2014). Nonsteroidal anti-inflammatory drugs have devastating adverse effects ranging from gastric irritation and ulcers to hepatotoxicity and

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renal failure when administered chronically(Khan et al., 2016). Although a large number of synthetic drugs used in the treatment of inflammation-related diseases have adverse effects such as: gastric damage, tolerance and dependence; the risk of recurrence of symptoms after discontinuation of treatment limits their use (Upton, 2015; Ezejaet al., 2011). Therefore, in this field, attention has been focused on the choice of natural agents derived from medicinal plants with less significant side effects and good efficacy against inflammation and pain (Babu et al., 2009; Mata et al., 2016). In recent years, the trend has been given to the study of natural products and healthy foods because of their potential as a source of biological assets and their possible contribution to the prevention of certain diseases (Mata et al., 2016). In this respect, the tests evaluating the toxicity of these natural products are extremely important to assess the risk incurred. In practice, pharmaco-toxicological evaluation generally includes studies of acute, subchronic, chronic, carcinogenic, genotoxic and reproductive effects (Jothyet al., 2013). The trial of treatment with economically accessible medicinal plants would be an alternative for the management of infections. The use of these medicinal plants by traditional healers and the satisfactory results that have resulted in some cases have led some countries, mainly African, to reflect on the revaluation of phytotherapy. However, for most of them, the scientific evidence is not always clear. Adjanohoun and de Souza (1976) identified nearly 501 species used in traditional medicine. Adjanohoun(2000), listed 814 species belonging to 130 botanical families with medicinal properties including Annona senegalensis, Detariummicrocarpum, Sarcocephaluslatifoliusand Combretumglutinosum. The phytochemistry (quantitative and qualitative) of these drugs revealed the presence of bioactive molecules capable of having analgesic, anti-inflammatory and bacterial properties Eyog et al (1999). It is therefore necessary to verify by a pharmacological study the analgesic and anti-inflammatory activity of the hydroethanolic extracts of leaves ofAnnona senegalensis, Sarcocephaluslatifolius, Combretum glutinosum and of Detariummicrocarpumcompared to a reference molecule and study their acute toxicity in vivo.

Material and Methods:-

Plant material: -

It is made up of the leave of the four plants species (DetariummicrocarpumGuill. &Perr;Annona senegalensis Pers. ssp.; Sarcocephaluslatifolius (Sm.) E. A. Bruce and Combretum glutinosum (Perr. Ex De). The leaves were collected in the commune of Kandi, Department of Alibori, Benin. They have been authenticated respectively under the vucher YH756/HNB, YH754/HNB, YH757/HNB, YH755/HNB by the National Herbarium of Benin, University of Abomey-Calavi, Benin. These leaves were dried at 25°C for two weeks. After drying, they were reduced to powder in the laboratory using a Retsch mill type SM 2000/1430/Upm/Smfet, Germany. The powders were used for the preparation of the hydroethanolic extract.

Animal material and acclimatization conditions: -

The animal material used was female Wistar rats of EOPS (Exempt from Specific Pathogenic Organisms) health status, approximately eight weeks old and weighing between 150g and 200g. The animals were housed in polypropylene cages integrated with water pots and under hygienic conditions with standard rat food and free access to water. After two weeks of acclimatization at a constant temperature of 22±2°C under a 12/12h light/dark cycle, the rats were divided into batches for the different tests. The body weight of the rats was recorded at the beginning and at the end of the experiment.

Preparation of extracts: -

The extracts were prepared according to the method described by Koudoroet al(2023). The powder (100 g) of each plant (D. microcarpum, A. senegalensis, S. latifoliusand C.glutinosum) was macerated for 48 h with continuous stirring in 500 ml of a mixture of water and ethanol (30:70/v:v). The macerates were then filtered 3 times with cotton and once with Whatman paper. The filtrates obtained were then evaporated using a rotary evaporator (IKA HB10S40, Germany) under reduced pressure. The concentrate was dried at 40°C in the oven until complete evaporation. The residues obtained after drying constitute the hydroethanolic extracts from each plant and have been used for the study of the various biological activities. The yield of crude hydroethanolic extract from each plant was determined by the ratio of the mass of the dry extract obtained to the mass of the plant material treated.

In-vivo anti-inflammatory activity: -

The experimental model of acute inflammation of the rat paw induced by 2% formalin was used according to the protocol used by Roko et al (2019). Rats were randomly assorted and bodily marked for indication. A number of 24 rats were divided into 6 groups of 4 rats each according to their body weight and fasted 15 hours before the experiment. All animals were provided with food and water adlibitum throughout the experimental period. The

diameter (Do) of the right hind paw of each rat was measured one hour before the various treatments using an electronic display caliper. The treatment was done orally (gavage) as follows:

1. Group 1 : served as negative control, received only physiological water at the rate of 1 ml per 100 g of body weight;
2. Group 2 : served as reference and received a reference anti-inflammatory, diclofenac at 50 mg/kg of body weight;
3. Group 3 : received 200 mg/kg of body weight of A. senegalensis hydroethanolic extract;
4. Group 4 : received 200 mg/kg of body weight of D. microcarpum hydroethanolic extract;
5. Group 5 : received 200 mg/kg of body weight of S. latifolius hydroethanolic extract;
6. Group 6 : received 200 mg/kg of body weight of C. glutinosum hydroethanolic extract.

One hour after gavage, 0.1 ml of a 2% formalin solution was injected into each rat, under the footpad of the right hind paw. Paw diameter at the arch of the foot was measured every hour until the fifth hour. The percentage increase (EIP) and inhibition (EAP) of edema were calculated from the following formulas:

$$EIP = \frac{Dt - Do}{D_t} \times 100$$

Where D_t: mean diameter of the right hind paw at time; Do: mean diameter of the right hind paw at time 0 (before treatment)

$$EAP = \frac{[(EIP)controlgroup - (EIP)treatedgroup]}{(EIP)controlgroup} \times 100$$

Analgesic activity evaluation:-

The analgesic effect of plants extract was assessed using the method described bySyet al (2009). Six groupsof 4 rats each were formed and treated using a gastric tube after 16 hours of fasting, as follows:

-Group 1 (Control): received physiological water at the dose of 1 mL/100g of body weight;

-Group 2 (Reference) : received acetylsalicylic acid at a dose of 200 mg/kg, per os;

-Group 3, 4, 5, 6 (Tests): received respectively hydroethanolic extract of D. microcarpum, A. senegalensis; S. latifoliusand C. glutinosum at 200 mg/kg per os.

Thirty (30) minutes after the various treatments, 0.1 mL of a 3% acetic acid solution was injected intraperitoneally for all the rats and the number of contortions (NC) for each rat was counted, over a period of 30 minutes. The percentage of inhibition of cramps (PIC) is calculated according to the following formula:

$$CIP = \frac{TCc - TCt}{TCc} \times 100$$

Where TCc: average of the number of twists of the control group;TCt: average of the number of twists of the treated groups.

Toxicological evaluation of the plant extract: -

Acute toxicity of plant extracts was evaluated in-vivo according to guidelines 423 of the Organization for Economic Co-operation and Development (OECD, 2002).

Adult Wistar rats used for toxicological evaluation received no other drug treatment during the experimental period apart from the plant extracts. After the acclimatization period, animals were divided into five groups of three animals (four experimental groups and one control group). Each group consist of 3 Wistar rats. The principle consists in administering the plants extracts to animals having the same food ration, orally and at a single dose of 2000 mg/kg of body weight. Thus, the treatment of the groups was done as follows:

1. Group 1: Rats receiving D. microcarpum hydroethanolic extract;
2. Group 2: Rats receiving A. senegalensishydroethanolic extract;
3. Group 3: Rats receiving S. latifolius hydroethanolic extract;
4. Group 4: Rats receiving C. glutinosum hydroethanolic extract;
5. Group 5: Rats receiving physiological water;

After the different treatments, animals were observed every 30 minutes for 8 hours on the first day and every day for 14 days. During this period, symptomatological disorders (agitation, lack of appetite, eye color, motor difficulties, diarrhea, lethargy and dyspnoea) are sought in Wistar rats.

On the 14th day after treatments, bloods from Wistar rats were collected by puncturing the retroorbital sinus of animals (under diethyl ether anesthesia). Blood samples were used for biochemical and hematological analyses, using BIOLABO diagnostic kits. Biochemical parameters investigated were:

Red Blood Cell; Hemoglobin; Hematocrit; Mean Corpuscular Volume; Level Corpuscular Hemoglobin Concentration; Mean Corpuscular Hemoglobin Concentration; White Blood Cell;Neutrophil; Eosinophil;Lymphocyte; Platelets; A.sen: Annona senegalensis; D. mic:Detariummicrocarpum; S. lat:Sarcocephaluslatifolius; C. glu: Combretum glutinosum

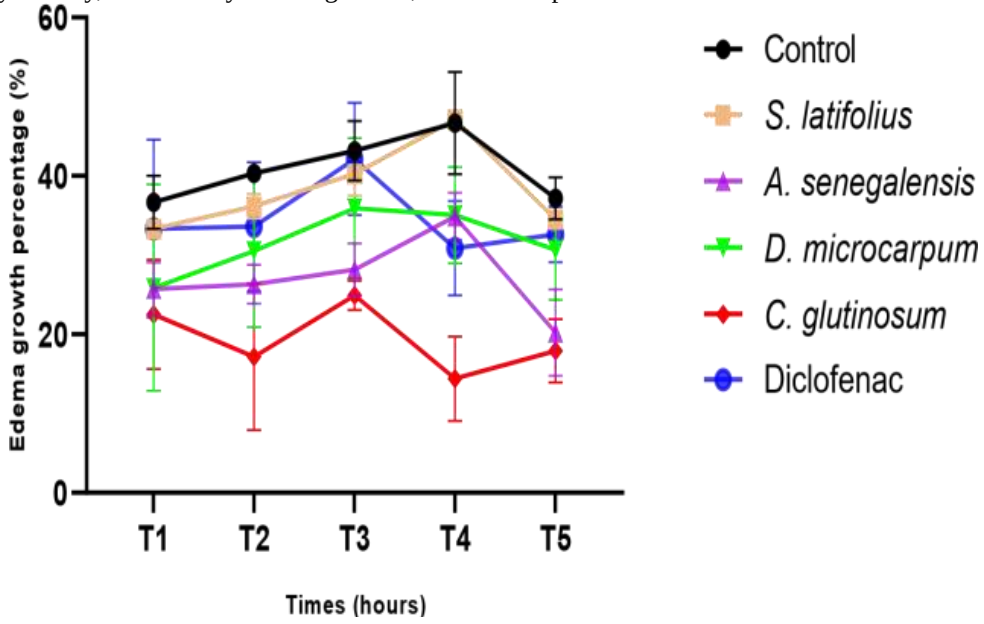
Statistical analysis: -

GraphPad Prism 9. 5. 1. (733) software was used to perform the graphs and statistical analysis of Biochemical parameters. A comparison of the means was carried out with the analysis of variances (ANOVA) followed by the multiple comparison test of Tukey. The differences are considered significant with $p < 0.05$ and very significant with $p < 0.001$.

Results:-

Anti-inflammatory activity of the tested extracts:-

Figure 1 presented results of the anti-inflammatory activity of the plant extracts. Results obtained indicated a very significant increase ($p<5\%$) in the volume of the paw of the rats of the control group with a maximum of 46.67±6.46% at the fourth hour. The administration of plant extracts at 200 mg/kg and diclofenac at 50 mg/kg prevents edema ($p< 0.0001$) in treated rats, compared to control rats which received only physiological water. The level of prevention is a function of time. Indeed, already after 1 hour of treatment, there is an inhibition of edema which varies from 8.90 ± 5.99% (S. latifolius) to 37.47 ± 24.53% (C. glutinosum). This inhibition is more important at the fourth hour when the hydroethanolic extract of C. glutinosum inhibits the increase in edema up to 68.03 ± 15.85% compared to diclofenac which recorded a percentage inhibition of 34.10±3.62%. Moreover, only the extract of A. senegalensis showed the highest percentage inhibition (44.94±18.61%) at the fifth hour after treatments. The comparative action of the extract effect of the different plants and of the reference molecule (diclofenac) showed that, at the second hour (T2), a difference is observed between the action of S. latifolius and C glutinosum ($p= 0.013$) on the one hand and between C. glutinosum and diclofenac ($p = 0.042$) on the other hand. At the third hour (T3), no difference ($p > 0.05$) was observed between the power of action of the extracts and that of the diclofenac used as the reference molecule. Moreover, at the fourth hour (T4) a difference between S. latifolius and C. glutinosum ($p = 0.001$), betweenA. Senegalensisand C. glutinosum ($p=0.026$), between D. microcarpum and C. glutinosum ($p = 0.027$) were observed. At the fifth hour (T5), only diclofenac and C. glutinosum showed a change ($p = 0.047$). In sum, the plant extract of C. glutinosum was found to be more effective with significant anti-inflammatory activity, followed by A. senegalensis, D. microcarpum and S. latifolius.



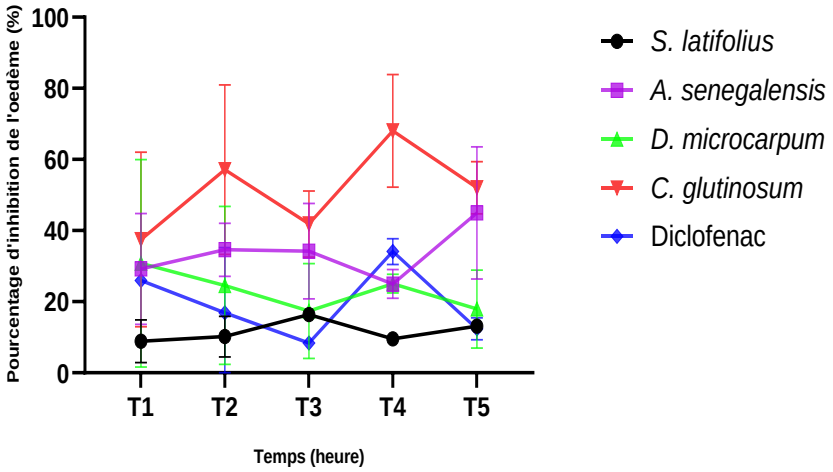


Figure 1:- Evolution of the percentage of edema growth [a] and edema inhibition [b] on rat paws.

Analgesic activity: -

The analgesic activity of the hydroethanolic extracts of the four plant species are presented in Table 1. Results obtained indicated that the administration of acetylsalicylic acid and the hydroethanolic extract of the four plants at a concentration of 200 mg/kg.bw significantly prevented ($p < 0.05$) the pain in rats, with important reduction of the number of contortions in the treated rats. Indeed, the number of contortions recorded with the extracts is significantly lower ($p < 0.05$) than that obtained with aspirin used as reference molecule. Treatment with A. senegalensis extract showed the lowest number of writhings (10.00±1.41) followed by D. microcarpum (11.00±1.31) and S. latifolius (18.00 ±3.83), as well as C. glutinosum (37.00±3.10). The hydroethanolic extract of the four plants is more effective than the aspirin used as a reference molecule which reduced the number of contortions to 43.00 ± 6.36.

Table 1:- Effect of plants extracts on pain induced by 3% acetic acid in rats.

	Control	**Reference**	**Extract of plants**			
Parameters	physiological water	Aspegic	D. microcarpum	A. senegalensis	S. latifolius	C. glutinosum
NbrCont	79.00±7.07^{a}	43.00±6.36^{ab}	11.00±1.31^{b}	10.00±1.41^{b}	18.00±3.83^{b}	37.00±3.10^{ab}
Inhibition(%)	nd	45.07±3.13^{ab}	85,37±15.63^{b}	87.37±0.65^{b}	76.96±5.64^{b}	54.74±35.33^{ab}

Legends: NbreCont: number of contorsion, nd : not determined, D. microcarpum: Detariummicrocarpum, A. senegalensis : Annona senegalensis ; S. latifolius : Sarcocephaluslatifolius ; C. glutinosum : Combretum glutinosum

Acute Toxicity:-

Figure 2 presented the results of rat's weight evolution after traitments. Analysis of variance of obtained results showed no change in the body weight of traited animals. These results indicated that the treatment did not affect the physical appearance of the animals and thus constitutes an indication of the safety of the extracts.

Control

A. Sen

C. glu

D. mic

S. lat

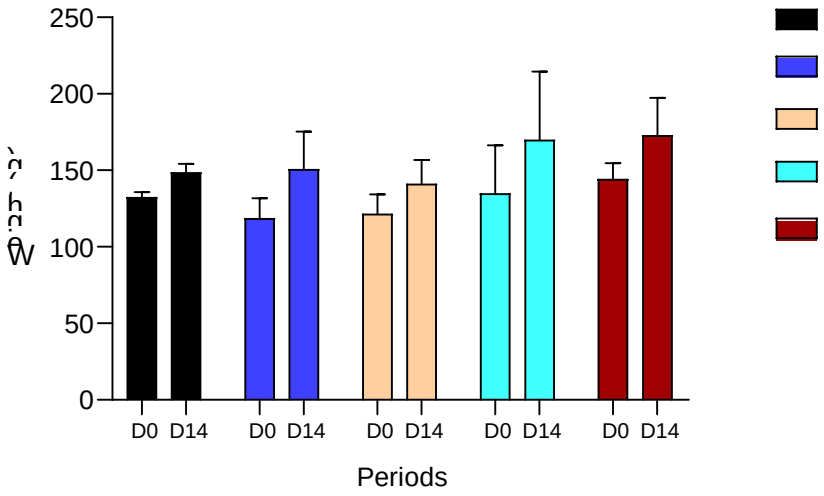


Figure 2: -Rats weight evolution after 14 days of traitment with the plant extracts.

Legends: A. sen : Annona senegalensis ; D. mic : Detariummicrocarpum; S. lat : Sarcocephaluslatifolius; C. glu : Combretum glutinosum

Effect of plant extracts on hematological parameters:-

The results of the hematological parameters are presented in Table 2. The analysis of results obtained showed that there is no variation (p > 0, 05) between most hematological parameters, when compare to the control these observations indicated that the treatment with the plant extracts does not induce any toxicity in the blood parameters of the treated rats.

Table 2: -Variation of hematological parameters.

Parameters	Control	A. sen	C. glu	D. mic	S. lat	P-value
RBC	6.28±1.30	7.62±0.36	7.67±0.02	7.32±1.47	7.53±1.10	p > 0.05
Hb	13.25±1.48	13.9±0.14	13.95±0.07	13.45±1.48	13.10±0.00	p > 0.05
Hte	50.50±7.77	52.5±0.70	50.0±0.70	52.5±7.77	52.5±3.53	p > 0.05
MCV	70.00±2.82	68.00±2.83	69.5±6.36	72.00±4.24	70.00±5.65	p > 0.05
LCHC	18.5±0.70	18.00±0.00	18.5±0.70	18.00±0.00	18.00±0.00	p > 0.05
MCHC	26.5±0.70	26.5±0.70	27.5±0.70	25.5±0.70	25.5±0.70	p > 0.05
WBC	7.80±2.36	4.48±1.58	7.18±0.38	8.70±0.94	6.62±0.50	p > 0.05
Neut	43.5±19.09	39.5±24.74	51.5±9.19	56.00±4.24	48.5±9.19	p > 0.05
Eos	2.00±1.41	5.5±3.53	1.5±0.70	4.00±2.82	2.00±1.41	p > 0.05
Lym	22.5±10.60	27.00±22.62	16.00±0.00	14.00±0.00	16.5±4.94	p > 0.05
Plaq	825.00±83.43	900.5±50.20	940.00±53.74	908.5±36.06	893.00±11.31	p < 0.001

Legends: RBC:Red Blood Cell ;Hb :Hemoglobin ; Hte : Hematocrit ; MCV: MeanCorpuscular Volume ; LCHC :LevelCorpuscularHemoglobin Concentration ; MCHC: MeanCorpuscularHemoglobin Concentration ; WBC: White Blood Cell ; Neut: Neutrophil ; Eos: Eosinophil ; Lym : Lymphocyte ; Plaq : Platelets ; A. sen : Annona senegalensis; D. mic : Detariummicrocarpum; S. lat : Sarcocephaluslatifolius; C. glu : Combretumglutinosum

Effect of plant extracts on the rat hepatic parameters

The results of the hepatic parameters investigation are shown in figure 3. The action of the extracts on the hepatic function was carried out by measuring the enzymatic activity of the transaminases, Alanine amino transferase (ALAT) and Aspartate amino transferase (ASAT). Results obtained shows that the treatment did not cause any variation ($p > 0.05$) in the transaminase rate (ASAT and ALAT) between the control and the treated groups.

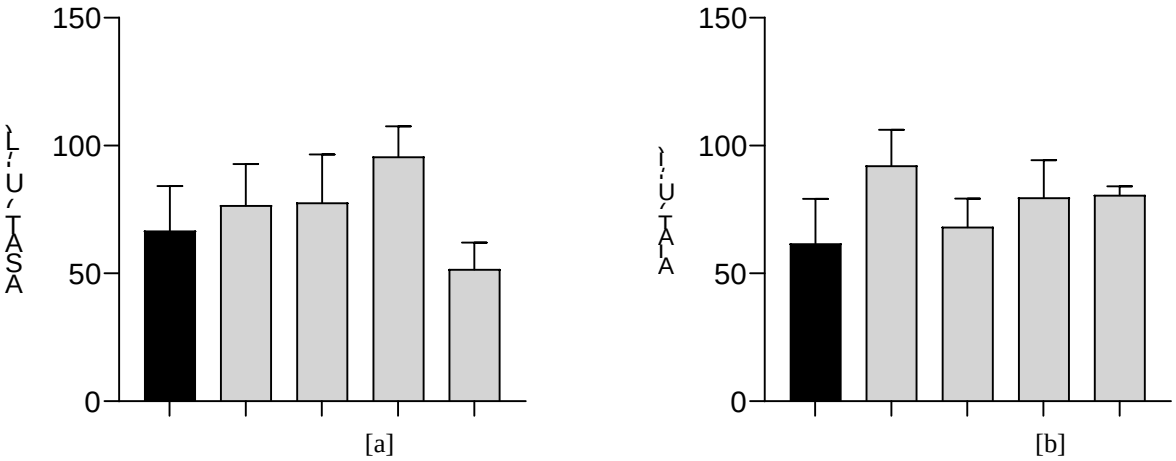
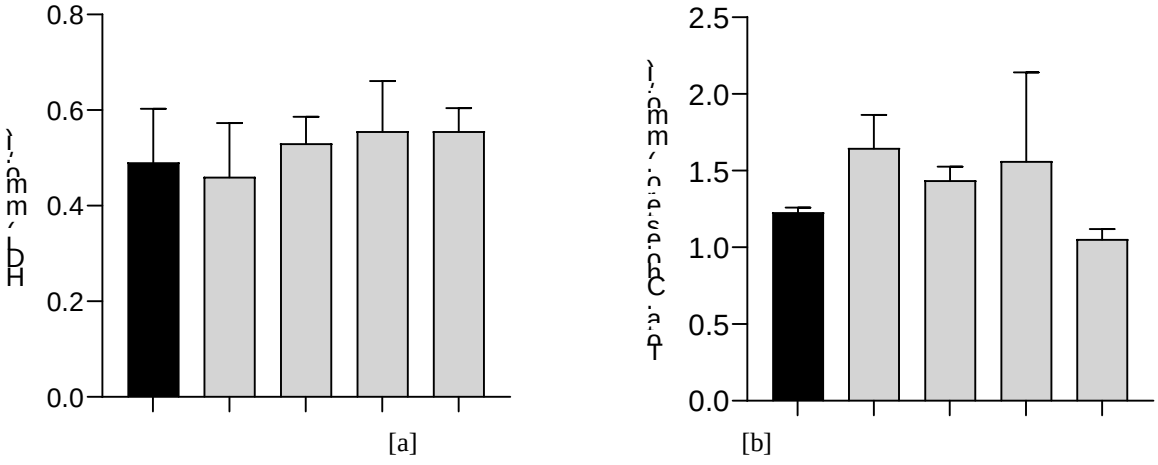


Figure 3:-Variation in ASAT [a] and ALAT [b] transaminases of Wistar rats.

A. sen : Annona senegalensis; D. mic : Detariummicrocarpum; S. lat : Sarcocephaluslatifolius; C. glu : Combretum glutinosum

Effect of plant extracts on the rats lipid profile:-

The effects of the plant extracts on the lipid profile variation is presented in figure 4. The analysis of obtained results indicated that the overall non-variation ($p > 0.05$) between the lipid parameters. Compared to the negative control group that received no treatment, the StudentNewman-Keuls (SNK) test shows that individuals treated with A. senegalensis and S. latifolius extract presented variation ($p = 0.04$) in total cholesterol. Indeed, the extract of A. senegalensis showed the highest total cholesterol content (1.64±0.21 mmol/L) while S. latifolius showed the lowest total cholesterol content (1.05± 0.07 mmol/L). Regarding the Triglyceride content, the control group presented the lowest content (0.66 ± 0.16 mmol /l) while the group treated with the D. microcarpum extract showed the highest content in triglyceride (0.88±0.09 mmol/L). Similarly, the D. microcarpum extract showed the highest HDL content (0.55±0.10 mmol/L), compared to the C. glutinosum extract which showed the lowest HDL content (0.46 ±0.11mmol/L).



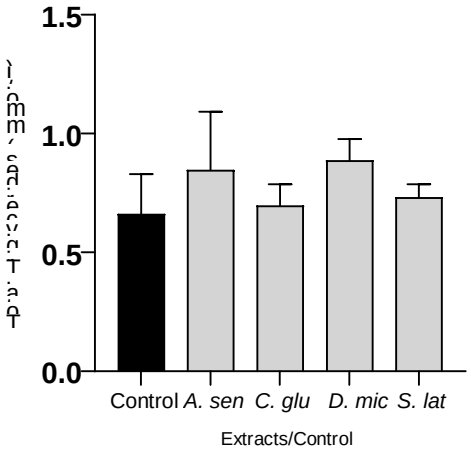


Figure 4:- Lipids profil variation HDL [a], Total Cholesterol [b] and Triglyceride [c] des rats A. sen : Annona senegalensis ; D. mic : Detariummicrocarpum; S. lat : Sarcocephaluslatifolius; C. glu : Combretum glutinosum

Effect of plant extracts on the rats renal function: -

The effect of the plant extracts on the variation in urea and creatine content is shown in Figure 5. The analysis of results indicated that there is no variation ($p > 0.05$). This observation shows that the various treatments have no effect on the kidneys of rats. However, the urea content increased by 0.19±0.03 g/L (D. microcarpum), 0.20±0.01 g/L(control), 0.25±0.07 g/L (A. senegalensis), 0.26±0.02 g/L (C. glutinosum) and 0.35±0.28 g/L (S. latifolius). Furthermore, the highest creatine content (9.90±5.23 mg/L) was obtained with the S. latifolius extract while the lowest content (7.05±0.35 mg/L) was obtained with the control.

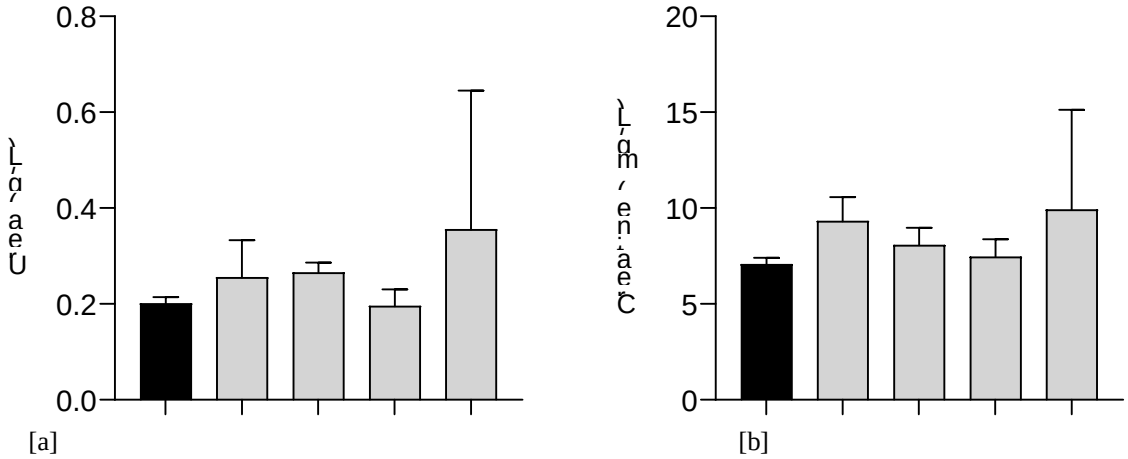


Figure 5:-Variation in urea [a] and creatine [b] content in control and treated rats, A. sen : Annona senegalensis ; D. mic : Detariummicrocarpum; S. lat : Sarcocephaluslatifolius; C. glu : Combretum glutinosum

Discussion:-

Inflammation is a complex physiological process associated with pain as a secondary process to inhibit the spread of infection. It is a multifaceted biological response of vascular tissues to harmful stimuli such as pathogens, damaged cells, physical and chemical insults, as well as immunological responses (Rahman et al. 2019). When it comes to humanity and health, understanding inflammation and associated processes has been a major enigma (Wanja, 2016). In our study, the oral administration to rats of hydroethanolic extracts of Annona senegalensis, Detariummicrocarpum, Sarcocephaluslatifoliusand Combretum glutinosumat a dose of 200 mg/kg proved to be significantly effective ($p < 0.05$) in the prevention of inflammatory edema induced by 2% formalin. Formalin is

widely used as an experimental tool for the induction of pain responses in mice. It causes a tonic pain sensation based on dependent concentration (Lopeset al., 2019). The mechanism of formalin-induced pain is mainly due to the release of histamine, serotonin and prostaglandins; and regulation of gene expression of tachykinin receptor 1, 5-hydroxytryptamine receptor 2A, Fos, and opioid receptor-1-like receptor (Maniet al., 2022). Diclofenac sodium is one of the most common drug choices for the treatment of acute inflammation and pain that works by inhibiting the cyclooxygenase (COX) pathway and thereby preventing the synthesis of prostaglandin and other eicosanoids (Ahmedet al., 2020). The same observation was made for rats treated with our hydroethanolic extracts of Annona senegalensis, Detariummicrocarpum, Sarcocephaluslatifoliusand Combretum glutinosum. We can conclude that our extracts, at a dose of 200mg/kg act in the same way as diclofenac. The anti-inflammatory activity of the plants (A. senegalensis, D. microcarpum, S. latifolius and C. glutinosum) studied could be attributed to the secondary metabolites, in particular the flavonoids contained in the extracts of these plants. Indeed, several studies have already shown that plant extracts rich in flavonoid compounds seem to inhibit the activity of the COX enzyme (Chahdouraet al., 2017)

Centrally and peripherally acting analgesics such as morphine, aspirin, indomethacin and diclofenac potentially reduce pain sensations, but these drugs also have significant side effects (Mani et al., 2022). In our study, the extracts inhibited cramps with a percentage ranging from 54.74% to 87.37%. This percentage of inhibition is greater than that of aspirin (45.07%) used as reference molecule. Treatment with our plant extracts resulted in a decrease in writhing in rats. Indeed, the number of contortions recorded with the extracts is significantly lower ($p < 0.05$) than that obtained with aspirin used as reference molecule. Treatment with A. senegalensis extract showed the lowest number of writhings (10.00±1.41) followed by D. microcarpum (11.00±1.31) and S. latifolius (18.00 ±3.83), then C. glutinosum (37.00±3.10). The hydroethanolic extract of the four plants is more effective than the aspirin used as a reference molecule. This result could be explained by the fact that our extracts inhibited the synthesis and release of various endogenous inflammatory mediators and the suppression of the sensitivity of peripheral nociceptors in free peritoneal nerve endings for induced pain by chemicals. These proposed mechanisms are consistent with the stated principles, any agent that decreases the number of writhings will demonstrate analgesia by inhibiting PG synthesis and release, and inhibiting peripheral pain transmission (Yimeret al., 2020). Moreover, the possible mechanism of the analgesic effects of our extracts can also be explained by the activation of the periaqueductal gray matter (PAG) to release endogenous peptides (i.e. endorphin or enkephalin). These endogenous peptides descend to the level of the spinal cord and function as inhibitors of the transmission of pain impulses at the level of the dorsal horn synapse or via peripheral mechanisms involved in the inhibition of PG, leukotrienes and other endogenous substances that play a key role in the central transmission of pain (Badoleet al., 2012). The analgesic effects of the extracts may be due to the presence of these aforementioned and identified phytoconstituents. This suggestion is in line with the work of Tadiwos et al (2017). These authors showed that phytoconstituents such as alkaloids, flavonoids, steroids and tannin isolated from medicinal plants possess significant analgesic activity. The results obtained from the present study corroborated the findings of others studies Tadiwos et al (2017);Geremewet al (2015) who demonstrated the analgesic and anti-inflammatory activities of herbal medicines in a dosedependent manner. In general, it can be concluded that the anti-inflammatory and analgesic activity of hydroethanolic extracts of A. senegalensis, D. microcarpum, S. latifoliusand C. glutinosum may be due to the cumulative effects of the presence of different active phytoconstituents in reducing synthesis, the release and action of the various endogenous inflammatory mediators mentioned above which play key roles in the development and progression of acute and subacute inflammation.

Conclusion:-

The tested plants extracts possess peripheral analgesic activity and central pain inhibition potential. It also showed anti-inflammatory activity. These results could imply that the plant extract was involved in the inhibition of various endogenous inflammatory mediators, pain transmission and mediators, due to the presence of secondary metabolites including alkaloids, flavonoids, saponins, terpenoids, tannins and essential oils which are repeatedly reported to possess analgesic and anti-inflammatory activities. The current findings provide scientific evidence on the claimed traditional uses of A. senegalensis, D. microcarpum, S. latifoliusand C. glutinosum for painful conditions and for inflammation purposes in Ethiopian folk medicines.

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